

REMARKS

Claims 25-29 are pending in the application. The Examiner has raised the following rejections:

- I. Claims 25-29 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention; and
- II. Claims 25-29 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cleary, *et al.*, (“Cleary”) in view of Levy, *et al.*, (“Levy”) and Embleton, *et al.* (“Embleton”).

These rejections will be addressed in the order listed above.

I. The Claims are not indefinite.

The Examiner has rejected Claims 25-29 under 35 U.S.C. §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention (Office Action, page 2). In particular, the Examiner asserts that it is not clear from the claims how the identification of a cell or clone relates to the claimed multivalent composition. Applicant respectfully disagrees. As indicated in the claim, a composition made according to the process of the claim comprises at least one individual clone that expresses the recited combinations of V_H and V_L regions. Nonetheless, for business reasons and without acquiescing to the Examiner’s arguments, and reserving the right to prosecute the original or similar claims in the future, Applicant has herein amended Claims 25, 28 and 29 to recite “wherein said multivalent composition comprises said expressed V_H and V_L regions.”

The Examiner has asserted that the claims are unclear regarding whether “said V_H and V_L regions” must include at least two V regions that differ by at least one idiotypic. Applicants respectfully disagree. The claims clearly indicate that the recited

nucleic acids comprise genes encoding any one of the following combinations of variable regions:

- 1) at least one V_H region and at least two V_L regions;
- 2) at least two V_H regions and at least one V_L region,
- 3) at least two V_H regions and at least two V_L regions.

The claims further specify that where there are at least two V_L regions, these regions differ by at least one idiotope, and where there are at least two V_H regions, these regions differ by at least one idiotope. The claims further recite that the sequences encoding “said V_H and V_L” regions are introduced into a parent cell line to generate a transformed cell line that expresses “said V_H and V_L” regions.

Nonetheless, for business reasons and without acquiescing to the Examiner’s arguments, and reserving the right to prosecute the original or similar claims in the future, Applicant has herein amended Claims 25, 28 and 29 to recite that “said clone capable of growth expresses a combination of V_H and V_L regions selected from the group consisting of at least one V_H region and at least two V_L regions, at least two V_H regions and at least one V_L region, and at least two V_H regions and at least two V_L regions, wherein said at least two V_L regions differ by at least one idiotope, wherein said at least two V_H regions differ by at least one idiotope.” As such, it is clear that each individual clone identified in this fashion has received at least two copies of V_H or V_L regions, such that the two copies differ by at least one idiotope.

For the reasons described above, Applicant submits that Claims 25-29 as amended are not indefinite under 35 U.S.C. §112, and respectfully requests that this rejection be removed.

II. The Claims are Not Obvious

The Examiner has rejected Claims 25-29 under 35 U.S.C. §103(a) as allegedly being unpatentable over Cleary, *et al.*, (“Cleary”) in view of Levy, *et al.*, (“Levy”) and Embleton, *et al.* (“Embleton”).

Prima facie obviousness requires: 1) a suggestion or motivation in the references or the knowledge generally available to combine or modify the reference teachings; 2) a

reasonable expectation of success should the suggested combination or modification take place; and 3) a teaching or suggestion of all the limitations of the claims. A showing of obviousness will fail if any one of these elements is not met. See, *e.g.*, MPEP § 2143. Applicant submits that the combination of the Cleary, Levy and Embleton references fails on all three elements.

The Examiner admits that Cleary does not teach a multivalent idiotypic composition comprising Vh sequences that comprising more than one idio type, or VI regions comprising more than one idio type (Office Action page 4). Levy is provided as corroborating Cleary. (Office Action page 5). Levy does not teach or suggest the multivalent compositions of the present invention.

The Examiner asserts that it would have been obvious to combine the Cleary and Levy references with the teachings of Embleton regarding improvements in the PCR cloning of immunoglobulin genes from B-lymphocytes which preserves the natural pairing of heavy chain and light chain and avoids the problem of screening artificial combinations. (Office Action page 5). Applicant respectfully disagrees.

1) Nothing in these references suggests such a combination and the Examiner has not pointed to anything in the knowledge generally available that suggests the combination. In fact, Embleton teaches *away* from making such a combination to make the compositions of the present invention. Embleton teaches methods particularly directed at amplifying immunoglobulin genes from within single cells, so as to avoid mixtures comprising the DNA of mixed populations of cells. See, *e.g.*, Abstract and second column on page 3831. In contrast, the compositions of the present invention of are made by using nucleic acid isolated from a population of tumor cells. See, *e.g.*, step (b) of Claim 25. Further, the multivalent compositions of the present invention are made by co-expressing variable regions derived from different cells in individual clone cells. This is contrary to the teachings of Embleton, which is directed toward preserving original V-gene combinations and avoiding such artificial combinations during expression of the isolated V-genes. As such, the method of Embleton does not teach or suggest the use of the Embleton method to produce the multivalent compositions of the present invention.

2) One of skill in the art would have no expectation of success in making the

claimed multivalent compositions by the method of Embleton. The method of Embleton is taught as a method of avoiding co-expressing variable regions derived from different cells. In contrast, the compositions of the present invention comprise such co-expressed variable regions. Thus, one of skill would not expect that use of the method of Embleton on the tumor cells described by Cleary and Levy would result in the multivalent compositions of the present invention.

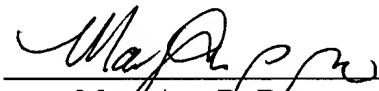
3) Because the method of Embleton teaches away from multivalent compositions and neither Levy nor Cleary teach such multivalent compositions at all, the combination cannot teach or suggestion of all the limitations of the claims.

For the reasons described above, Applicant submits that the combination of Cleary, Levy, and Embleton does not establish obviousness of the instant claims and respectfully requests that this rejection be removed.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all reasons for rejection should be removed and Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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